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HELLER EHRMAN WHITE & MCAULIFFE LLP 275 MIDDLEFIELD ROAD MENLO PARK, CA 94025-3506			HUYNH, PHUONG N	
		ART UNIT	PAPER NUMBER	
		1644		

DATE MAILED: 11/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/000,439	SAXON, ANDREW
Examiner	Art Unit	
Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE Three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 24 August 2004.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-59 is/are pending in the application.
4a) Of the above claim(s) 35-39 and 45-59 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-34 and 40-44 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 2/12/02; 10/22/04.
4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
5) Notice of Informal Patent Application (PTO-152)
6) Other: *Figure 9: sequence alignment.*

DETAILED ACTION

1. Claims 1-59 are pending.
2. Applicant's election with traverse of Group 1, Claims 1-34 and 40-44 drawn to an isolated fusion molecule wherein the autoantigen is myelin basic protein, filed 8/24/04, is acknowledged. The traversal is on the grounds that independent claim 1 and dependent claims 2-34 and 40-44 are drawn to the same invention. As explained throughout the specification, a specific embodiment of the invention concerns fusion molecules in which a first polypeptide sequence is capable of specific binding to a native IgG inhibitory receptor comprising an ITIM motif, functionally connected to a second polypeptide sequence which sequence is an antigen. This fusion molecule is capable of indirectly binding to a native IgE receptor through a third polypeptide sequence. The third polypeptide sequence includes an immunoglobulin specific for the antigen sequence that binds to a native IgE receptor (FcER). Accordingly, all of the fusion molecules claimed contain a common structure, i.e. the first polypeptide sequence. Secondly, the second polypeptide sequence in all of the fusion molecules is similar in that it is an antigen. The fusion molecules share a common utility since they are designed to treat autoimmune diseases and they share a common feature, the first polypeptide sequence. There is not a serious burden on the examiner if restriction is not required. Claim 1 is linking species. The Examiner should have more properly requested Applicant to elect a species in claims 1-34 and 40-44 for examination, rather than restricting the claims between inventions. Applicant notes that the Examiner has indicated that where applicant elects claims directed to a product and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP 821 .04.

The request for rejoinder of process claims in the event that the product claim are subsequently found allowable is acknowledged. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. In response to applicant's argument that all of the fusion molecules contain a

common structure, i.e. the first polypeptide sequence, the second polypeptide sequence in all of the fusion molecules is similar in that it is an antigen. The fusion molecules share a common utility since they are designed to treat autoimmune diseases and they share a common feature, the first polypeptide sequence. This is not found persuasive because of the reasons set forth in the restriction mailed 2/26/04. Further, the instant specification does not disclose that these fusion molecules would be used together to treat the same autoimmune disease. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation such as inhibition of allergen specific IgE as opposed to increase the half life of the antigen, or different effects such as treating multiple sclerosis as opposed to treating allergy (MPEP § 806.04, MPEP § 808.01). Unity of invention applies only to application filed under 35 U.S.C. 371. Instant application is a US application and not PCT entering US under 35 U.S.C. 371. Therefore, unity of invention does not apply in this case. Finally, a prior art search also requires a literature search. It is a burden to search more than one invention. Therefore, the requirement is still deemed proper and is therefore made FINAL.

3. Claims 35-39, and 45-59 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.
4. Claims 1-34 and 40-44, drawn to an isolated fusion molecule wherein the autoantigen is myelin basic protein, are being acted upon in this Office Action.
5. The disclosure is objected to because of the typographical error “pAN1782” on page 78, line 22. It should have been “pAN1872”.
6. The drawing Figure 9, filed 10/24/01, is not approved because the halftone of the figure is too dark and one cannot see the detail of the vessel. Please see enclosed Figure 9. Appropriate action is required.
7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-34 and 40-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) an isolated fusion molecule comprising hinge-CH2-CH3 of human IgG1 constant region consisting of SEQ ID NO: 1 fused to a full length myelin basic protein comprising SEQ ID NO: 12 or a peptide from myelin basic protein consisting of SEQ ID NO: 13, and (2) an isolated fusion molecule comprising hinge-CH2-CH3 of human IgG1 constant region consisting of SEQ ID NO: 1 fused to human IgE constant region CH2-CH3-CH4 domains for inhibiting IgE mediated release of histamine, **does not** reasonably provide enablement for any fusion molecule as set forth in claims 1-34 and 40-44. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only an isolated fusion molecule comprising a hinge-CH2-CH3 of human IgG1 constant region consisting of SEQ ID NO: 1 fused to a full length myelin basic protein comprising SEQ ID NO: 12 or a peptide from myelin basic protein consisting of SEQ ID NO: 13, and (2) an isolated fusion molecule the hinge-CH2-CH3 of human IgG1 constant region consisting of SEQ ID NO: 1 fused to human IgE constant region CH2-CH3-CH4 domains of SEQID NO: 7 for inhibiting IgE mediated release of histamine.

The specification does not teach how to make and use all fusion molecule comprising any first polypeptide sequence functionally connected to any second polypeptide sequence through any third polypeptide sequence, any fusion molecule wherein the second sequence comprises any antigen sequence, any portion of any autoantigen sequence, any autoantigen such as any IgE class antibody, any rheumatoid arthritis autoantigen, any multiple sclerosis autoantigen, any type I diabetes mellitus autoantigen and any portion thereof such as the ones recited in claims 7-8 because a fusion molecule without the amino acid sequence has no structure, much less function.

Stryer *et al* teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

Ngo *et al*, PTO 1449, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Further, there is insufficient guidance as to which “portion” of which autoantigen in the fusion molecule is effective for treating which autoimmune disease. The term “comprises” in claim 4 is open-ended. It expands the undisclosed autoantigenic epitope to include additional amino acids at either or both ends of the autoantigen sequence in the claimed fusion molecule. There is a lack of guidance as to which amino acids to be added.

With regard to percentage of sequence identity (claims 9, 15, and 18-21), in addition to the lack sequence for the first, second and third polypeptides in the fusion molecule mentioned above, there is insufficient guidance as to which amino acids within the full-length polypeptide can be modified and yet maintain its function. It is known in the art that the relationship between the amino acid sequence of a protein (polypeptide) and its tertiary structure (i.e. its binding activity) are not well understood and are not predictable (see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz, et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495). There is no recognition in the art that sequence with identity predicts biological function. It is known in the art that even a single amino acid changes or differences in a protein's amino acid sequence can have dramatic effects on the protein's function. Mikayama *et al.*, teach that the human glycosylation-inhibiting factor (GIF) protein differs from human macrophage migration inhibitory factor (MIF) by a single amino acid residue (Figure 1 in particular). Yet, Mikayama *et al.* further teach that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF bioactivity (Abstract in particular). It is also known in the art that amino acid sequence determines the function of the polypeptide or protein. However, the predictability of which changes can be tolerated in an amino acid sequence and still retain similar functions and properties requires a knowledge of, and guidance such as which amino acids within the full-length polypeptide are tolerant of modification and which amino acid residues are conserved or less tolerant to modification in which the product's structure relates to its functional usefulness. The use of “percent” in conjunction with any of the various terms that refer to

sequence identity or similarity is a problem because sequence identity between two sequences has no common meaning within the art. The term “percent” is relative and can be defined by the algorithm and parameter values set when using the algorithm used to compare the sequences. The scoring of gaps when comparing one sequence to another introduces uncertainty as to the percent of similarity between two sequences.

Because applicants have not disclosed the specific condition used to score sequence identity while using any computer program, it is unpredictable to determine which amino acid sequences of autoantigen in the claimed fusion molecule will have at least about 90% identity to the which native autoantigen and still retains its function (claim 9). Without guidance as to which amino acids within the full-length polypeptide are tolerant of modification, it would take undue amount of experimentation to arrive at the claimed invention. Likewise, it would require undue experimentation for one of skill in the art to identify polypeptide that merely has 85%, 95%, 95% or 98% sequence identity to SEQ ID NO: 3 (claims 18-21) and maintains functional activity. A sequence identity of 85% to SEQ ID NO: 3 means that there is at least 15% or about 35 amino acids differences. There is insufficient guidance as to which amino acids within SEQ ID NO: 3 can be modified by addition, deletion, substitution and combination thereof and still maintain its function such as binding to native IgG inhibitory receptor, in turn, the fusion molecule would be useful for treating any autoimmune diseases.

Attwood *et al.* teach that protein function is context-dependent and the state of the art of making functional assignments merely on the basis of some degree of similarity between sequences and the current structure prediction methods is unreliable (See figure, entire document).

Skolnick *et al.*, PTO 1449, teach that sequence-based methods for function prediction are inadequate and knowing a protein’s structure does not tell one its function (See abstract, in particular). A polypeptide having at least about 80% identity to SEQ ID NO: 3 means at least about 90 amino acid differences. Given the unlimited number of undisclosed fusion molecules, there is insufficient working example demonstrating that all fusion molecules are effective for treating all autoimmune diseases. It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions could result in substantially different biological or pharmacological activities. Even if the fusion molecule is limited to human Fc fused to the myelin basic protein, there is a lack of in vivo working example demonstrating that the fusion is effective for treating multiple sclerosis.

Blanas *et al* (Science 274: 1707-1709, Dec 1996; PTO 1449) teach treating autoimmune rheumatoid arthritis and multiple sclerosis by oral administering autoantigen could lead to onset of autoimmune diabetes (see abstract, in particular).

Couzin *et al* teach that finding the telltale antibodies doesn't guarantee that autoimmune diabetes will strike (See page 1863, Science 300: 1862-65, 2003). Couzin *et al* teach that three major prevention trials have failed to stop autoimmune disorder such as type I diabetes (See entire document).

Mackay *et al*, PTO 1449, teach that two recent phase I clinical trial for treatment of multiple sclerosis by administering myelin basic protein peptide resulted in exacerbations of multiple sclerosis (See page 346, col. 2, in particular).

A pharmaceutical composition comprising any fusion molecule in the absence of in vivo is unpredictable for the following reasons: (1) the fusion molecule may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the fusion molecule may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the fusion molecule unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of *Ex parte Aggarwal*, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

With regard to claims 10 and 25, since the amino acid sequence of the autoantigen sequence in the fusion molecule is not enabled, it follows that the nucleic acid encoding said autoantigen in the fusion molecule is not enabled. Further, there is insufficient guidance as to which nucleic acid hybridizes to the complement of which nucleic acid molecule encoding which native autoantigen, much less which stringer conditions should be used. The same reasoning applies to claim 25. It is known that hybridization conditions are sequence dependent and will be different with different parameters, i.e. salt concentration, organics, melting points, annealing temperature. The state of the prior art as exemplified by Wallace *et al*, PTO 1449, is such that determining the specificity of hybridization probes is empirical by nature and the effect of mismatches within an oligonucleotide probe is unpredictable.

Claim 17 is included in this rejection because the second and third polypeptide in the fusion molecule is not enabled for the reasons discussed *supra*.

With regard to claims 22-23 and 24, the term “comprises” is open-ended. It expands the hinge of a human IgG1 constant region to include additional amino acids at either ends of the first polypeptide within the claimed fusion molecule. There is a lack of guidance as to which amino acids to be included. Further, the first polypeptide would include the whole IgG rather than just the constant region of the human IgG1 because the term “comprise” is recited in said claims.

Claims 26-30 are included in this rejection because the first, second and third polypeptide in the fusion molecule are not enabled for reasons discussed above.

With regard to claims 31-34, the term “comprises” is open-ended. It expands the polypeptide linker to include additional amino acids at either or both ends. There is a lack of guidance as to which amino acids to be included. Given the indefinite number of undisclosed “fusion molecule”, it is unpredictable which undisclosed “fusion molecule” is effective for treating which autoimmune diseases. Since the fusion molecule is not enabled, it follows that the pharmaceutical composition and article of manufacture comprising said fusion molecule are not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of *Ex parte Aggarwal*, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

9. Claims 1-34 and 40-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of all fusion molecule comprising any first polypeptide sequence...functional connected to any second polypeptide sequence through any third polypeptide sequence as set forth in claims 1-34 and 40-44.

The specification discloses only an isolated fusion molecule comprising hinge-CH2-CH3 of human IgG1 constant region consisting of SEQ ID NO: 1 fused to a full length myelin basic protein comprising SEQ ID NO: 12 or a peptide from myelin basic protein consisting of SEQ ID NO: 13, and (2) an isolated fusion molecule comprising hinge-CH2-CH3 of human IgG1 constant region consisting of SEQ ID NO: 1 fused to human IgE constant region CH2-CH3-CH4 domains for inhibiting IgE mediated release of histamine.

With the exception of the specific fusion molecule mentioned above, there is insufficient written description about the structure associated with function of all fusion molecules comprising *any* “first polypeptide”...connected to *any* “second polypeptide” through *any* “third polypeptide” without the amino acid sequence. Further, there is insufficient written description about the structure associated with function of any second polypeptide such as any antigen sequence (claim 2), any autoantigen sequence (claims 3-4), any autoantigen sequence comprises at least one autoantigenic epitope (claim 4), any IgE class antibody (claim 6), any autoantigen sequence such as the ones recited in claims 7-8, any autoantigen sequence has at least 90% sequence identity to any native autoantigen sequence (claim 9), any autoantigen sequence encoded by any nucleic acid hybridizing under stringent conditions to the complement of any nucleic acid molecule encoding any native autoantigen (claim 10) in the claimed fusion molecule without the amino acid sequence. There is insufficient written description about which “portion” of which autoantigen sequence is part of the second polypeptide in the claimed fusion molecule (claim 3). In addition to the problem mentioned above, the term “at least 90% sequence identity” in claim 9 means there is at least 10% difference to which undisclosed native autoantigen in the claimed fusion molecule. There is inadequate written description about which amino acids within the full-length native autoantigen of the fusion molecule could be modified by substitution deletion, addition, and combination thereof and whether the resulting modified autoantigen in the fusion molecule maintains its structure and function. Since the autoantigen sequence (second polypeptide) in the fusion molecule is not adequately described, the nucleic acid encoding said autoantigen and the stringent hybridization condition in claim 10 are not adequately described.

Likewise, there is also insufficient written description about the structures of any first polypeptide such as any amino acid sequence at least 85% identity with a native human IgG heavy chain constant region sequence in the claimed fusion molecule (claim 15), any amino acid sequence at least 85%, 90%, 95%, 98% sequence identity to SEQ ID NO: 3 without the amino acid sequence (claims 18-21). Further, the term “at least 85%, 90%, 95%, 98% sequence

“identity” means there is at least 15%, 10%, 5% and 2% differences in the first polypeptide of the fusion molecule. There is inadequate written description about which amino acid within the full-length sequence of the first polypeptide of the fusion molecule can be modified by addition, deletion, substitution and combination thereof and it still maintains function. The term “comprises” in claims 15-25 expands the first polypeptide sequence (immunoglobulin Fc region) in the fusion molecule to include additional amino acids at either or both ends. There is lack of written description about which amino acids to be added. Since the term “comprises” could read on the full length IgG Fc, the fusion molecule comprising the complete IgG Fc fused to any second polypeptide through any third polypeptide is not been described in the specification as filed. With regard to claim 25, in addition to the problem of “comprises”, there is also inadequate written description about the nucleic acid sequence hybridizing to which portion of the complement of the IgG heavy chain constant region of SEQ ID NO: 1, much less about the “stringent hybridization condition” in the claimed fusion molecule given the hybridization condition is sequence dependent.

Adequate written description requires more than a mere statement that it is part of the invention. The amino acid sequence itself for the fusion molecule is required. Until the amino acid sequences of the first, second and third polypeptides in the fusion protein have been described, the fusion molecule is not adequately described. Since the fusion molecule is not adequately described, it follows that the pharmaceutical composition and article of manufacture comprising said fusion molecules are not adequately described.

Further, the specification discloses only three fusion molecules wherein the fusion molecule comprises a hinge-CH2-CH3 from only human IgG1 constant region consisting of SEQ ID NO: 1 fused to only myelin basic protein comprising SEQ ID NO: 12 (full length) or a peptide from myelin basic protein consisting of SEQ ID NO: 13 or a human IgE constant region consists of CH2-CH3-CH4 domains, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of fusion molecule to describe the genus for the claimed method. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Art Unit: 1644

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 12-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The “said IgE receptor” in claims 12 and 13 has no antecedent basis in base claim 11 because the word “said IgE receptor” is not recited in claim 11. Claim 11 recites IgG receptor.

The “Fc ϵ RI IgG receptor” in claim 12 is indefinite because Fc ϵ RI is an IgE receptor, not IgG receptor as claimed.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-4, 9-11, 15-16, 22-28, 32-34, and 40-41 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,420,247 (May 30, 1995; PTO 892).

The ‘247 patent teaches an isolated fusion molecule comprising a first polypeptide such as human IgG Fc constant region functionally connected to a second autoantigen polypeptide sequence such as human LIFR that is capable specific binding to LIF ligand through a third polypeptide sequence such as a polypeptide linker (See Figure 3, col. 12, line 36, col. 14, lines 43-52, col. 13, line 55-63, claim 4 of ‘247 patent, in particular). The reference native human Fc constant region is from IgG1 that comprises at least part of the hinge region. The reference IgG Fc constant region inherently is capable of binding to a native IgG inhibitory receptor such as low affinity Fc γ RIIb IgG receptor that comprises the an immune receptor-based inhibitory motif (ITIM) (See col.14, line 26-66, in particular). Since the reference first polypeptide is the same as the claimed first polypeptide in the claimed fusion molecule, the amino acid sequence encoded by a nucleic acid would inherently hybridize under stringent conditions to at least a portion of the complement of the IgG heavy chain constant region nucleotide sequence of claimed SEQ ID NO: 1. The reference polypeptide linker such as (Gly4Ser) n where n is 4, which is within the claimed range of about 5 to about 25 amino acid residues. The reference linker sequence comprises

asparagine amino acid residues and inherently these asparagines are also an endopeptidase recognition motif (see col. 13, line 57-63, in particular). The '247 patent further teaches a pharmaceutical composition comprising the reference fusion molecule in admixture with a pharmaceutically acceptable excipient such as sucrose (See col. 21 lines 66 bridging col. 22, lines 1-30, in particular). The '247 patent teaches that IgG Fc fusion molecule can easily be purified using protein A or protein G affinity chromatography (See col. 33, lines 35-47, in particular). Claims 21-24 are included in this rejection because the term "comprises" is open-ended. It expands the IgG to include additional amino acid to include the hinge, CH₂, CH₃ domains. Thus, the reference teachings anticipate the claimed invention.

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.
15. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
16. Claims 1, 3, and 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,420,247 (May 30, 1995; PTO 892) in view of WO 95/14779 (June 1995, PTO 892), Basu *et al* (J Biol Chem 268(18): 13118-27, June 1993; PTO 1449) and Daeron *et al* (J Clin Invest 95(2): 577-85, Feb 1995; PTO 892).

The teachings of the '247 patent have been discussed *supra*. The '247 patent teaches that IgG Fc fusion molecule can easily be purified using protein A or protein G affinity chromatography (See col. 33, lines 35-47, in particular).

The claimed invention in claim 1 differs from the teachings of the reference only in that the fusion molecule wherein the second polypeptide is capable of specific binding to a native IgE receptor (FcεR).

The claimed invention in claim 12 differs from the teachings of the reference only in that the fusion molecule wherein the IgE receptor is a high affinity FcεRI IgE receptor.

The claimed invention in claim 13 differs from the teachings of the reference only in that the fusion molecule wherein the IgE receptor is a high affinity FcεRII (CD23) IgE receptor.

The WO 95/14779 publication teaches human IgE Fc (hIgE-Fc) comprising the second, third and fourth constant region domains (Cε2-Cε4) (See page 1, second full paragraph, Abstract, Figure 1, in particular), which are useful in the treatment of allergy conditions (See page 5, first paragraph, in particular).

Basu *et al* teach that the Fc region of human IgE comprises C epsilon 2, C epsilon 3 and C epsilon 4 domains that are sufficient for binding to the alpha chain of the high affinity IgE receptor with high affinity similar to native IgE and that the Fc region of IgE can inhibit the release of histamine from cells expressing human Fc epsilon RI (high affinity receptor).

Daeron *et al* teach that IgE induced mediator release is inhibited by crosslinking FcεRI to FcγRIIb1 or FcγRIIb1, which are low affinity receptors. The inhibition of receptors is useful for desensitization in allergic patients (See page 577, column 1, page 579, column 2, Figures 3a-3b, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to substitute the LIF-R in the fusion molecule as taught by the '247 patent for the human IgE heavy chain constant region that binds to an high affinity IgE receptor (FcεRI) as taught by the WO 95/14779 publication and Basu *et al* and low affinity IgE receptor (FcεRII) as taught by Daeron *et al* for a fusion molecule comprising a first polypeptide IgG heavy chain constant region that capable of binding to IgG inhibitory receptor such as low affinity FcγRIIb connected to an IgE heavy chain constant region sequence that is capable of binding to an IgE receptor such as high affinity receptor (Fc epsilon RI) or low affinity receptor (Fc epsilon RII) as taught by the '603 patent, the WO 95/14779 publication and Basu *et al* through a third polypeptide linker sequence as taught by the '247 patent to inhibit IgE induced mediator release. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because Daeron *et al* teach that IgE induced mediator release can be inhibited by crosslinking Fc ϵ RI to Fc γ RIIb1 or Fc γ RIIb1 which are low affinity receptors and is useful for desensitization in allergic patients (See page 577, column 1, page 579, column 2, Figures 3a-3b, in particular). The WO 95/14779 publication teaches human IgE Fc (hIgE-Fc) comprising the second, third and fourth constant region domains (C ϵ 2-C ϵ 4) (See page 1, second full paragraph, Abstract, Figure 1, in particular), which are useful in the treatment of allergy conditions (See page 5, first paragraph, in particular). Basu *et al* teach that the Fc region of IgE comprising C epsilon 2, C epsilon 3 and C epsilon 4 domains is sufficient for binding to the alpha chain of the high affinity IgE receptor with high affinity similar to native IgE and the Fc region of IgE which can block the release of histamine from cells expressing human Fc epsilon RI. The '247 patent teaches that IgG Fc fusion molecule can easily be purified using protein A or protein G affinity chromatography (See col. 33, lines 35-47, in particular).

17. Claims 1-3, and 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,420,247 (May 30, 1995; PTO 892) in view of Warren *et al* (Proc Natl Acad Sci USA 92: 11061-65, November 1995; PTO 892).

The teachings of the '247 patent have been discussed *supra*. The '247 patent teaches that IgG Fc fusion molecule can easily be purified using protein A or protein G affinity chromatography (See col. 33, lines 35-47, in particular).

The claimed invention as recited in claim 7 differs from the teachings of the reference only in that the fusion molecule wherein the autoantigen sequence is multiple sclerosis autoantigen.

The claimed invention as recited in claim 8 differs from the teachings of the reference only in that the fusion molecule wherein the autoantigen sequence is multiple sclerosis autoantigen myelin basic protein (MBP).

Warren *et al* teach autoantigen sequence such as myelin basic protein (see Figure 3, page 11063, in particular) and various antigenic epitopes or fragment thereof such as MBP 84-93, MBP89-95 (see page 11062, col. 2, in particular). The reference autoantigen is found in multiple sclerosis (see title, page 11065, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to substitute the LIF-R in the fusion molecule as taught by the '247 patent for

autoantigen such as myelin basic protein (MBP) as taught by Warren *et al* for a fusion molecule comprising a first polypeptide IgG heavy chain constant region that capable of binding to IgG inhibitory receptor such as low affinity Fc γ RIIb connected to myelin basic protein through a polypeptide linker as taught by the '247 patent and Warren *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because the '247 patent teaches that IgG Fc fusion molecule can easily be purified using protein A or protein G affinity chromatography (See col. 33, lines 35-47, in particular).

18. Claims 1-4 15, and 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,420,247 (May 30, 1995; PTO 892) in view of US Pat No 5,565,335 (Oct 1996; PTO 892).

The teachings of the '247 patent have been discussed *supra*.

The claimed invention in claim 18 differs from the teachings of the reference only in that the fusion molecule wherein the first polypeptide sequence comprises an amino acid sequence having at least 85% identity to amino acid sequence of SEQ ID NO: 3.

The claimed invention in claim 19 differs from the teachings of the reference only in that the fusion molecule wherein the first polypeptide sequence comprises an amino acid sequence having at least 90% identity to amino acid sequence of SEQ ID NO: 3.

The claimed invention in claim 20 differs from the teachings of the reference only in that the fusion molecule wherein the first polypeptide sequence comprises an amino acid sequence having at least 95% identity to amino acid sequence of SEQ ID NO: 3.

The claimed invention in claim 21 differs from the teachings of the reference only in that the fusion molecule wherein the first polypeptide sequence comprises an amino acid sequence having at least 98% identity to amino acid sequence of SEQ ID NO: 3.

The '335 patent teach various fusion molecule comprising a first polypeptide such as human IgG1 Fc having an amino acid sequence at least 97.2% identical to the claimed SEQ ID NO: 3 (See reference SEQ ID NO 7, in particular) fused to a second polypeptide such as autoantigen CD4, myelin associated glycoprotein (See col. 4, Detailed description, lines 18-31, in particular). The reference Fc fusion molecule enhances the plasma half-life of the fusion molecule and is useful for (see Summary of invention, col. 5, lines 26-47, Table IV, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to substitute the Fc polypeptide in the fusion protein as taught by the '247 patent for the human IgG1 Fc having an amino acid sequence at least 97.2% identical to the claimed SEQ ID NO: 3 (See reference SEQ ID NO 7, in particular) as taught by the '335 patent for a fusion molecule comprising a human IgG Fc constant region functionally connected to any second autoantigen polypeptide sequence such as human LIFR, or myelin associated protein or CD4 through a third polypeptide sequence such as a polypeptide linker as taught by the '247 patent and the '335 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because the '247 patent teaches that IgG Fc fusion molecule can easily be purified using protein A or protein G affinity chromatography (See col. 33, lines 35-47, in particular). The '335 patent teach that Fc fusion molecule enhances the plasma half-life of the fusion molecule and is useful for (see Summary of invention, col. 5, lines 26-47, in particular). Claims 21-24 are included in this rejection because the term "comprises" is open-ended. It extends the claimed at least part of the CH2 and CH3 domains of native human IgG1 constant region to the complete IgG Fc region as taught by the '355 patent or the '247 patent.

19. Claims 1, and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,420,247 (May 30, 1995; PTO 892) in view of Elias et al (J Biol Chem 265(26): 15511-17, September 1990; PTO 892) and Marks et al (J Cell Biol 135(2): 341-354, Oct 1996; PTO 892).

The teachings of the '247 patent have been discussed *supra*.

The claimed invention in claim 29 differs from the teachings of the reference only in that the fusion molecule comprises at least one amino terminal ubiquitination target motif.

The claimed invention in claim 30 differs from the teachings of the reference only in that the fusion molecule comprises at least one proteasome proteolytic signal, wherein said signal is selected from the group consisting of large hydrophobic amino acid residues, basic amino acid residues, and acidic amino acid residues.

The claimed invention in claim 31 differs from the teachings of the reference only in that the fusion molecule comprises at least one

Elias et al teach N terminal residue of the protein is one important structural determinant recognized by ubiquitin ligase to conjugated protein to ubiquitin for protein degradation (See page col. 15511, col. 2, second paragraph, in particular). Elias et al teach protein with hydrophobic amino acid residues such as leucine, or basic amino acid residues such as histidine, arginine and lysine determines the half-life of the protein (See paragraph, bridging page 15511 and 15512, in particular).

Marks et al teach that adding ubiquitination target motif such as bulky hydrophobic group di-leucine motif to any protein would target the protein to the lysosome or endosomal compartments for antigen processing (See abstract, page 348, in particular).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to add at least one amino terminal ubiquitination target motif such as large hydrophobic amino acid residue such as leucine as taught by Elias and Marks to the fusion molecule as taught by the '247 patent to target the transmembrane protein such as Ig Fc connected to LIF-R through a peptide linker to route the fusion molecule to the lysosome and endosome antigen processing as well as modulating the modulate the half-life of the fusion molecule as taught by the '247 patent, Elias et al and Marks et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art at the time the invention was made would have been motivated to do this because Elias et al teach adding hydrophobic amino acid residues such as leucine, or basic amino acid residues such as histidine, arginine and lysine to the amino terminal modulates the half-life of the protein (See page 1552, col. 1, in particular). Marks et al teach that that adding ubiquitination target motif such as bulky hydrophobic group di-leucine motif to any protein would target the protein to the lysosome or endosomal compartments for antigen processing to be release from the cell (See abstract, page 348, in particular).

20. Claims 1, 3, and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,420,247 (May 30, 1995; PTO 892) in view of US Pat No 5,945,294 (Aug 1999, PTO 892).

The teachings of the '247 patent have been discussed supra.

The claimed invention in claims 42-44 differs from the teachings of the reference only in that an article of manufacture comprising a container, a fusion molecule within the container, and a label or package insert on or associated with the container.

The '294 patent teaches diagnostic kit (for IgE detection using human Fc epsilon receptor (See abstract, in particular). The kit is useful for diagnosing abnormal conditions in animals that are associated with changing levels of IgE associated with allergy (See column 15, lines 19-23, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the human Fc epsilon receptor as taught by the '294 patent for the fusion protein as taught by the '247 patent in the kit for diagnostic assays. One would have been motivated, with a reasonable expectation of success to do this for convenience and commercial expedience. A kit will allow for ease of use for the practitioner since all the necessary reagents, standard and instructions for use are included in a kit as taught by '294 (See column 14, in particular). From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Claim 44 is included in this rejection because a product is a product, irrespective of its intended use.

21. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

22. Claims 1-3, 11-28, and 40-44 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 77, 79-81, 83-89 and 96 of copending Application No. 09/847,208. Although the conflicting claims are not identical, they are not patentably distinct from each other because the following reasons.

Claim 1 of instant application recites an isolated fusion molecule comprising a first polypeptide sequence capable of specific binding to a native IgG inhibitory receptor comprising an immune receptor tyrosine-based inhibitory motif (ITIM), functionally connected to a second polypeptide sequence capable of specific binding, through a third polypeptide sequence, to native IgE receptor (FcER), wherein said first and second polypeptide sequences are other than antibody variable region sequences and wherein said fusion molecule is not capable of T cell interaction prior to internalization (genus).

Claim 77 of 09/847,208 recites An isolated fusion molecule comprising a human IgG heavy chain constant region sequence capable of binding to a human IgG inhibitory receptor directly functionally connected to a human IgE heavy chain constant region sequence capable of binding to a human IgE receptor wherein said fusion molecule is capable of binding both the IgG inhibitory receptor and the IgE receptor and claim 81 of 09/847,208 recites the fusion molecule of claim 77 comprising a human IgG heavy chain constant region sequence capable of binding to a human IgG inhibitory receptor directly functionally connected to a human IgE heavy chain constant region sequence capable of binding to a human IgE receptor wherein said fusion molecule is capable of binding both the IgG inhibitory receptor and the IgE receptor wherein said IgG heavy chain constant region sequence and IgE heavy chain constant region sequence are connected via a polypeptide linker of 15 to 25 amino acid residues (species). Species anticipates a genus. Likewise, the same reasoning applies to claims 89 and 96 of 09/847,208.

Claim 11 of instant application recites the fusion molecule wherein said inhibitory receptor is a low affinity Fc γ RIIb IgG receptor, which is the same IgG inhibitory receptor as recited in claims 83 of 09/847,208.

Claim 12 of instant application recites the fusion molecule wherein said IgE receptor is a high affinity Fc ϵ RI IgE receptor which is the same high affinity Fc ϵ RI IgE receptor recited in claim 84 of 09/847,208.

Claim 13 of instant application recites the fusion molecule wherein said IgE receptor is a low affinity Fc ϵ RII (CD23) IgE receptor which is the same low affinity Fc ϵ RII (CD23) IgE receptor recited in claim 83 of 09/847,208.

Claim 14 of instant application recites the fusion molecule wherein said Fc γ RIIb and Fc ϵ RI receptors are of human origin. The Fc γ RIIb and Fc ϵ RI receptors in claims 77, and 84 of 09/847,208 are also human origin.

Claim 15 of instant application recites the fusion molecule wherein said first polypeptide sequence comprises an amino acid sequence having at least 85% identity with a human IgG heavy chain constant region sequence. Since the human IgG heavy chain constant region of the fusion molecule in claim 77 of 09/847,208 is 100% identity to an amino acid sequence of a human IgG heavy chain constant region sequence, said human IgG heavy chain is at least 85% identical with a native human IgG heavy chain constant region sequence.

Claim 16 of instant application recites the fusion molecule wherein said IgG is selected from the group consisting of IgG1, IgG2, IgG3 and IgG4. The IgG2, IgG3 and IgG4 in the fusion molecule are the same as that of Claim 85 of 09/847,208 which recites the fusion molecule of claim 77 wherein said IgG is selected from the group consisting of IgG1, IgG2, IgG3 and IgG4.

Claim 17 of instant application recites the fusion molecule wherein said native human IgG heavy chain constant region sequence is the native human IgG heavy chain constant region sequence of SEQ ID NO: 2 (specie). Claim 86 of 09/847,208 recites the fusion molecule wherein the IgG heavy chain constant region is an IgG1 heavy chain constant region (genus). The specie (claim 17 of instant application) anticipates the genus of claim 86 of 09/847,208.

Claim 18 of instant application recites the fusion molecule of claim 17 wherein said first polypeptide sequence comprises an amino acid sequence having at least 85% identity to the amino acid sequence of SEQ ID NO: 3.

Claim 19 of instant application recites the fusion molecule of claim 17 wherein said first polypeptide sequence comprises an amino acid sequence having at least 90% identity to the amino acid sequence of SEQ ID NO: 3.

Claim 20 of instant application recites the fusion molecule of claim 17 wherein said first polypeptide sequence comprises an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 3.

Claim 21 of instant application recites the fusion molecule of claim 17 wherein said first polypeptide sequence comprises an amino acid sequence having at least 98% identity to the amino acid sequence of SEQ ID NO: 3. However, claim 88 of 09/847,208 recites the fusion molecule of claim 87 wherein the IgG1 heavy chain constant region is the amino acid sequence of SEQ ID NO: 3. The SEQ ID NO: 3 in claim 88 of 09/847,208 application would include the

amino acid sequence having at least 85%, 90%, 95%, and 98% identity to the amino acid sequence of SEQ ID NO: 3.

Claim 22 of instant application recites the fusion molecule of claim 21 wherein said first polypeptide sequence comprises *at least* part of the CH2 and CH3 domains of a native human IgG1 constant region. Claim 23 of instant application recites the fusion molecule of claim 22 wherein said first polypeptide sequence additionally comprises at least part of the hinge of a native human IgG1 constant region. Claim 87 of 09/847,208 recites the fusion molecule wherein said IgG1 heavy chain constant region sequence consists of the hinge-CH2-CH3 portion of an IgG1 heavy chain constant region. The at least part of the CH2 and CH3 domains of a native human IgG1 constant region in claims 22 and 23 of instant application would include the IgG1 heavy chain constant region sequence consists of the hinge-CH2-CH3 portion of an IgG1 heavy chain constant region of the fusion protein in claim 87 of 09/847,208 application. The same reasoning applies to claim 24 of instant application.

Claim 26 of instant of instant application recites the fusion molecule of claim 3 wherein said first and second polypeptide sequences are functionally connected through a linker and claim 27 of instant of instant application recites the fusion molecule of claim 26 wherein said linker is a polypeptide linker. Claim 28 of instant of instant application recites the fusion molecule of claim 27 wherein said polypeptide linker sequence consists of about 5 to about 25 amino acid residues. However, claim 79 of 09/847,208 application recites the fusion molecule comprising a human IgG heavy chain constant region sequence capable of binding to a human IgG inhibitory receptor directly functionally connected to a human IgE heavy chain constant region sequence wherein the IgG heavy chain constant region sequence and IgE heavy chain constant region sequence are connected via polypeptide linker consist of 5 to 25 amino acid residues. Claim 81 of 09/847,208 application recites the fusion molecule comprising a human IgG heavy chain constant region sequence capable of binding to a human IgG inhibitory receptor directly functionally connected to a human IgE heavy chain constant region sequence wherein the IgG heavy chain constant region sequence and IgE heavy chain constant region sequence are connected via polypeptide linker consist of 15 to 25 amino acid residues. The peptide linker of about 5 to about 25 amino acid residues of claim 26 of instant application would include the polypeptide linker consist of 5 to 25 or 15 to 25 amino acid residues of 09/847,208 application.

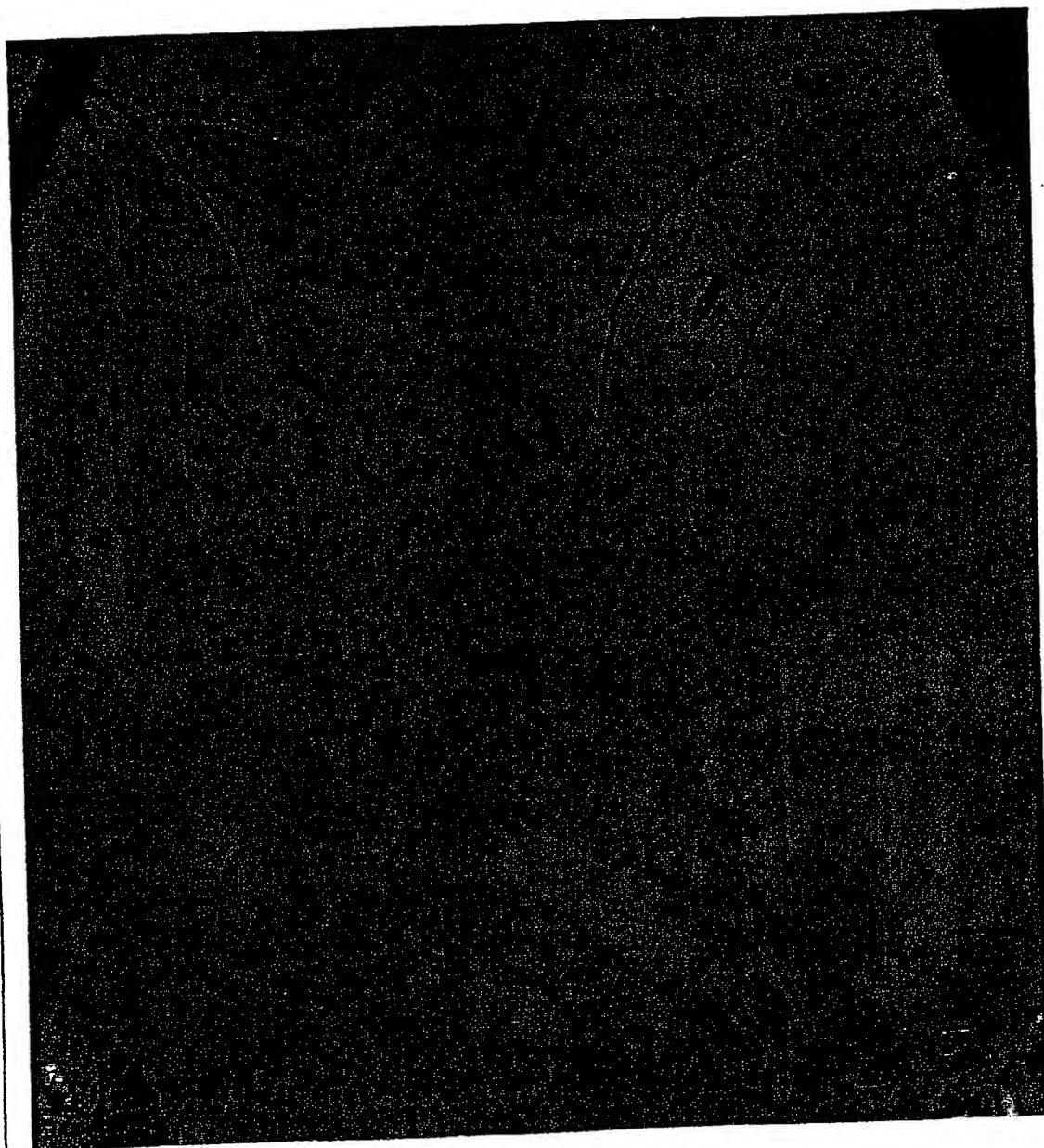
This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

23. Claims 5-6 and 17 are free of prior art.
24. No claim is allowed.
25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.
26. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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November 12, 2004

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FIGURE 9-



A: 250ng human IgE-anti NP
B: saline
C: 250ng human IgE-anti NP+250ng GE2
D: 250ng human IgE-anti NP+250ng PS IgE

APPLICANT: NAGATA, Shigeo kazu
TITLE OF INVENTION: NOVEL Fas ANTIGEN DERIVATIVE
FILE REFERENCE: 110-247P
CURRENT APPLICATION: US/09/180, 100
EARLIER APPLICATION NUMBER: PCT/JP97/01502
EARLIER FILING DATE: 1997-05-01
NUMBER OF SEQ ID NOS: 25
SOFTWARE: patentin Ver. 2.0
SEQ ID NO: 11
LENGTH: 360
TYPE: PRI
ORGANISM: Homo sapiens

US-09-180-100-11

Query Match 97.2%; Score 1225; DB 3; Length 360;
Best Local Similarity 97.0%; Pred. No. 6.3e-116; Matches 225; Conservative 3; Mismatches 4; Indels 0; Gaps 0;
QY 1 EPKSCDKTIVCPCPAPELIGGSVFLFPKPKDQTMISRTPEVTCVVVDDVSHEDEPEVK 60
Db 129 EPKSCDKTIVCPCPAPELIGGSVFLFPKPKDQTMISRTPEVTCVVVDDVSHEDEPEVK 188
QY 61 NWYDGVEVHNVKTPREEQNSTYRVVSLTVLHONWNGKEYKCKVSNKALPAPIECT 120
Db 189 NWYDGVEVHNVKTPREEQNSTYRVVSLTVLHONWNGKEYKCKVSNKALPAPIECT 248
QY 121 ISKAKVQPREPQVYTLPPRSDELTKNOVSILTCVKGTFPSDIAVEWESNGOPENNYKTP 180
Db 249 ISKAKGQPREPQVYTLPPRSDELTKNOVSILTCVKGTFPSDIAVEWESNGOPENNYKTP 308
QY 181 PVLDVGSPFLYSLTVKDSRQWQGQNFCSVMEALTHHYQORSLISLSPGK 232
Db 309 PVLDSDGSFLYSLTVKDSRQWQGQNFCSVMEALTHHYTOKSLSLSPGK 360

RESULT 6

US-08-336-311-7
Sequence 7, Application US/08236311
Patent No. 556535

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COMPUTER READABLE FORM:
MEDIUM TYPE: 5.25 inch, 360 Kb floppy disk

COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: patin (Genentech)

CURRENT APPLICATION DATA:

APPLICATION NUMBER: US/08/236, 311

FILING DATE: 02-MAY-1994

CLASSIFICATION: 435

PRIOR APPLICATION DATA:

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APPLICATION NUMBER: 07/842777

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APPLICATION NUMBER: 07/104329

FILING DATE: 02-OCT-1987

RESULT 6

US-08-457-918-7
Sequence 7, Application US/08457918
Patent No. 6117655

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MEDIUM TYPE: 5.25 inch, 360 Kb floppy disk

COMPUTER: IBM PC compatible
OPERATING SYSTEM: PC-DOS/MS-DOS
SOFTWARE: patin (Genentech)

CURRENT APPLICATION DATA:

APPLICATION NUMBER: US/08/457, 918

FILING DATE: 1-JUN-1995

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PRIOR APPLICATION DATA:

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APPLICATION NUMBER: 07/842777

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PRIOR APPLICATION DATA:

APPLICATION NUMBER: 07/250785

FILING DATE: 28-SEP-1988

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TELECOMMUNICATION INFORMATION:
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TELEX: 910/371-7168
INFORMATION FOR SEQ ID NO: 7:
SEQUENCE CHARACTERISTICS:
LENGTH: 371 amino acids
TYPE: amino acid
TOPOLOGY: linear

US-08-236-311-7

Query Match 97.2%; Score 1225; DB 1; Length 371;
Best Local Similarity 97.0%; Pred. No. 6.6e-116; Matches 225; Conservative 3; Mismatches 4; Indels 0; Gaps 0;
QY 1 EPKSCDKTIVCPCPAPELIGGSVFLFPKPKDQTMISRTPEVTCVVVDDVSHEDEPEVK 60
Db 140 EPKSCDKTIVCPCPAPELIGGSVFLFPKPKDQTMISRTPEVTCVVVDDVSHEDEPEVK 199
QY 61 NWYDGVEVHNVKTPREEQNSTYRVVSLTVLHONWNGKEYKCKVSNKALPAPIECT 120
Db 200 NWYDGVEVHNVKTPREEQNSTYRVVSLTVLHONWNGKEYKCKVSNKALPAPIECT 259
QY 121 ISKAKVQPREPQVYTLPPRSDELTKNOVSILTCVKGTFPSDIAVEWESNGOPENNYKTP 180
Db 260 ISKAKGQPREPQVYTLPPRSDELTKNOVSILTCVKGTFPSDIAVEWESNGOPENNYKTP 319
QY 181 PVLDVGSPFLYSLTVKDSRQWQGQNFCSVMEALTHHYQORSLISLSPGK 232
Db 320 PVLDSDGSFLYSLTVKDSRQWQGQNFCSVMEALTHHYTOKSLSLSPGK 371

RESULT 7

US-08-457-918-7
Sequence 7, Application US/08457918
Patent No. 6117655

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APPLICATION NUMBER: US/08/457, 918

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